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Histopathological analysis of a 15-year user of an auditory brainstem implant

Steven R. Otto, MA¹, Jean Moore, PhD³, Fred Linthicum, MD², William Hitselberger, MD⁴, Derald Brackmann, MD⁵, and Robert V. Shannon, PhD¹

¹Department of Communications and Auditory Neuroscience, Los Angeles, California

²Histopathology Department, Los Angeles, California

³House Research Institute, Los Angeles, California

⁴private practice, Los Angeles, California

⁵House Clinic, Los Angeles, California, U.S.A

Introduction

Auditory brainstem implants (ABIs) have been used to treat deafness in individuals with neurofibromatosis type 2 (NF2) since Drs. William House and William Hitselberger implanted the first device in 1979.^{1, 2} The Nucleus Multichannel ABI (Cochlear Corp., Centennial, CO) received approval from the US Food and Drug Administration in 2000, based on clinical trials approved by our institutional review board. One of the largest single populations of ABI recipients is at House Research Institute (HRI) in Los Angeles with 280 patients. Presently, there are also many individuals without NF2 who are benefiting from ABIs, including a substantial number of infants, very young children, and teens without viable peripheral auditory structures.^{3, 4}

At most ABI centers in the United States, implantation of the ABI is accomplished via a translabyrinthine approach when the patient's first- or second-side vestibular schwannoma is surgically removed. The electrode array is placed into the lateral recess of the fourth ventricle over the cochlear nuclear complex. Details of the procedure have been described elsewhere.⁵

About 6 weeks after implantation, patients return to our center for initial testing and activation of their ABIs, including assessment of auditory and/or nonauditory sensations, electrical thresholds and comfortable loudness levels, assessment of electrode-specific pitch percepts, and assessment of speech perception performance. Details regarding this have also been previously reported.⁶

In 1992, we had our first opportunity to acquire and examine the brainstem of a 5-year user of an early single-channel ABI, which did not indicate negative effects from ABI use.⁷ Recently, we had the opportunity to examine the brainstem of a 15-year multichannel ABI user who expired from causes related to NF2. This analysis sheds light on the long-term affects of the ABI on neural tissue, an issue that is particularly relevant for present and future pediatric recipients who are facing a lifetime of ABI use.

Case Report

In 1994 at the age of 29, the male patient with NF2 underwent surgery to remove a second-side vestibular schwannoma on his right side and received an ABI. About 6 weeks postoperatively, the patient returned to our center for initial testing and activation of his implant. The patient reported receiving sound on all eight implanted electrodes at relatively low levels of electrical stimulation. He also reported feeling a mild twitch in his right eye (not observable) on two electrodes and a slight feeling of dizziness on another electrode.

Also during the initial activation, the patient was asked to describe the quality and pitch of sounds on each electrode. He reported that they generally sounded like tones, and that each electrode sounded different in pitch. Using previously described techniques,⁵ we scaled and ranked the patient's electrode-specific pitch percepts and used this information to program his Spectra sound processor (Cochlear Corp., Centennial, CO). In this process, electrodes are assigned to specific frequency bands depending upon the spectral characteristics of input sound and the patient's own ranking of pitch sensations. The patient's initial sound processor program (map) is shown in Table I. Electrode 2 was not used due to the mild twitch sensation it caused in the patient's right eye.

Speech and environmental sound perception was evaluated at initial device activation to obtain a baseline for tracking performance. Regular perceptual testing included several recorded closed- and open-set tests. The tests were administered in sound-only mode (no lip-reading) with the exception of one sentence test (City University of New York Sentence Test [CUNY]), which was also administered with sound plus lip-reading.

The patient's initial speech perception scores are shown in Figure 1. These results were in the average range for initial stimulation, except the score on the CUNY Sentence Test in sound plus lip-reading mode was below average. This was due in part to the patient's NF2-related vision problems.

During regular follow-up visits, the patient reported that he generally used the ABI during all his waking hours, and that it was of great value in maintaining social contacts and in helping him keep his information technology job. We also periodically reprogrammed his sound processor to accommodate the typical changes in threshold and comfortable loudness levels, as well as in the pitch ranking. Over time, we were able to incorporate additional electrode combinations in his map that gave him additional pitch percepts and expanded his number of useable channels to 10. The last sound processor program is shown in Table II.

With experience, the patient's speech perception scores ultimately improved as much as 50% over initial device activation, including some sound-only (open-set) sentence recognition ability (Fig. 1). After a number of years of declining health due to NF2, this patient developed respiratory difficulties and eventually succumbed to pneumonia. He had previously signed documents to have his brainstem structures acquired by our Temporal Bone Bank at HRI, and these materials were analyzed to evaluate the number and health of neurons in the electrically stimulated region.

The temporal bones and brain stem of this subject were obtained through the HRI donor program. Following death due to respiratory failure, the body was refrigerated until the time of removal of the brain stem. The electrode array was apparently avulsed at the time of removal. The brain stem was subsequently stored in 10% neutral buffered formalin for several weeks prior to processing. During processing, a block containing the cochlear nuclei bilaterally was dissected out and embedded in celloidin. The specimen block was cut into 120- μ m-thick sections, which were stained with hematoxylin and eosin and mounted on numbered glass slides. Microscopic analysis was done with a Zeiss binocular microscope

model #034507 (Carl Zeiss AG, Oberkochen, Germany), and images were recorded with an Optronics digital camera (Optronics, Goleta, CA) through a Nikon Optiphot microscope (Nikon, Tokyo, Japan).

On examination of the histological sections, it was noted that the ependymal surface of the right cochlear nuclear complex had been torn loose. Because there was no sign of tissue reaction in the area, we believe this occurred postmortem when the electrode array was avulsed. Within both left and right nuclei there was good preservation of cell size, morphology, and packing density, allowing identification of the various types of cochlear neurons. Figure 2 shows the stimulated right side. Visual inspection revealed no clear differences between the stimulated and unstimulated sides. The excellent degree of neural preservation in this patient is consistent with our previous observations⁷ of less pathological change in auditory brainstem nuclei in subjects suffering from viral labyrinthitis, sensorineural hearing loss, or acoustic neuromas than in those whose deafness was caused by bacterial labyrinthitis or a genetic condition (Scheibe disorder).

The similarity in cell health between stimulated and unstimulated cochlear nuclei suggests that long-term chronic electrical stimulation of the human brainstem is neither harmful nor beneficial to neural preservation. This comparison must be tempered by the uncertainties as to the equality of the original states of the nuclei on the two sides. If we assume that the two sides were in similar condition following tumor removal and then again similar after 15 years of daily unilateral ABI use, then the ABI has not had either deleterious or beneficial effect on the cells of the cochlear nuclei. In our previous study,⁷ the degree of neural preservation was similar across sides in the cochlear nuclei as well as in higher auditory nuclei, including the inferior colliculus. Thus, long-term electrical stimulation (with a cochlear implant or ABI) in these cases did not seem to substantially affect neuronal health either negatively or beneficially.

A common finding of ABI centers around the world is that performance varies widely across recipients, with some users capable of understanding considerable speech without lip-reading cues. Correlates of ABI performance are of great interest and are under study at many of these centers. A number of factors can impact success. Good preservation of neuronal size, morphology, and density in the nuclei probably are fundamentally important, but many other factors (some medical/surgical) also are involved. For example, our clinical impression has been that high motivation to excel with an ABI can be of great significance, because it can impact how much time an ABI is used in daily communication. High motivation and experience may offset some deficiencies in other areas, such as neural preservation.

Our patient's electrical threshold and comfortable loudness levels were relatively low. This good electrical sensitivity, at relatively short pulse durations and the minimal presence of nonauditory sensations, suggested an excellent electrode array placement with good neural survival. This patient rather quickly developed into one of our better performers, and his auditory performance was stable for 15 years, suggesting that perceptually there were few if any negative effects from the long-term daily use of his ABI. Postmortem analysis of his cochlear nuclei confirms excellent cell survival and health, even after 15 years of daily electric stimulation. It is of interest to note that the auditory perception and performance of the first ABI recipient has been stable for more than 30 years.

Prolonged electrical auditory brain stem stimulation (at least 15 years) had no deleterious affect on cochlear nucleus neurons. This is a positive sign for long-term safety and efficacy in pediatric ABI recipients.

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Figure 1.

Speech perception test scores in percent correct (initial and latest testing) from a 15-year ABI user. SERT = Sound Effects Recognition Test; MTS Word = Monosyllable Trochee Spondee Test; NUCHIPS = Northwestern University Children's Perception of Speech Word Test; Consonants and Vowels = Iowa Consonant and Vowel Tests; CUNY Sents = City University of New York Sentence Test; S+V = sound plus vision mode; S = sound only mode; CID Sents = Central Institute for the Deaf Sentence Test.

Figure 2.
Section through the posteroventral cochlear nucleus on the right (implanted) side. Arrows indicate cochlear nuclei. Hematoxylin and eosin, 40 $\times$. eb = electrode array bed.

Table I

Initial Auditory Brainstem Implant Sound Processor Program

Active Electrode	Indifferent Electrode	Threshold Level	Comfort Level	Pulse Duration	Lower Frequency	Upper Frequency
Threshold and comfortable loudness levels are in clinical units from the Nucleus auditory brainstem implant programming software. Pulse durations are in microseconds per phase for biphasic charge-balanced pulses. Frequencies are in hertz.						
9	1	65	100	100	400	933
3	1	135	159	100	933	1,466
5	1	95	125	100	1,466	2,000
7	1	65	95	100	2,000	2,533
8	1	115	130	100	2,533	3,066
4	1	135	170	100	3,066	3,600
6	1	105	138	100	3,600	4,133

Table II

Latest Auditory Brainstem Implant Sound Processor Program

Active Electrode	Indifferent Electrode	Threshold Level	Comfort Level	Pulse Duration	Lower Frequency	Upper Frequency
Threshold and comfortable loudness levels are in clinical units from the Nucleus auditory brainstem implant programming software. Pulse durations are in microseconds per phase for biphasic charge-balanced pulses. Frequencies are in hertz.						
5	6	135	170	300	240	880
3	4	150	226	250	880	1,200
4	5	155	226	200	1,200	1,520
6	7	105	155	250	1,520	1,840
9	1	100	135	100	1,840	2,160
7	1	110	150	100	2,160	2,480
3	1	140	189	100	2,490	2,828
5	1	135	184	100	2,828	3,249
4	1	145	194	150	3,249	3,732
6	1	149	180	100	4,288	4,926